REMARKS

Substitute Specification

As required by 37 C.F.R. §1.125(a), a clean and a marked version of a Substitute Specification are enclosed. Please note the change of the title of the invention from "OPTICAL ARRANGEMENT IN THE ILLUMINATING BEAM OF A MICROSCOPE" (as stated on the Declaration and Power of Attorney and the Filing Receipt) to "OPTICAL ARRANGEMENT IN THE ILLUMINATION BEAM PATH OF A MICROSCOPE."

Claim Rejections - 35 U.S.C. §112

Claims 17, 22-25, 28-29, and 32-39 stand rejected under 35 U.S.C. §112, second paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. The Examiner rejected Claims 17 and 38 as containing a feature not supported by the specification, namely, "a focus of the zoom optical system remains at a location of said point-like source." The phrase "a focus of the zoom optical system remains at a location of said point-like source" has been deleted from Claims 17 and 38, making the present rejection moot with respect to Claims 17 and 38, and with respect to the claims dependent on Claims 17 and 38.

Claim 25 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite as Claim 25 depends upon itself. Claim 25 has been amended to depend from Claim 17, making Claim 25 definite. Withdrawal of the rejection of Claim 25 is courteously requested.

Claim Rejections - 35 U.S.C. §103

Claims 17, 24, 25, 32, 33, and 39 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamoto (United States Patent No. 5,184,012) in view of Hara et al. (Japanese Patent No. 5-107037). Claim 24 has been cancelled, making the rejection moot with respect to Claim 24. To the extent that the rejection may apply to newly amended Claim 17, the rejection is respectfully traversed for the following reasons.

Claim 17 recites, "a point-like light source operatively arranged to emit an illumination beam along said illumination beam path." Yamamoto discloses a laser source 1 that is not a point-like source. The Examiner has cited Hara et al. as disclosing a point-like source. However, there is no teaching, suggestion, or motivation in either Yamamoto or Hara to combine their teachings to create the present invention. In fact, Hara teaches away from the present invention. Hara discloses an optical arrangement wherein light from source 2 is expanded and collimated before it is incident on pupil 5. The beam is rectangular before it is incident on the circular pupil 5. Thus, Hara clearly teaches overillumination of pupil 5, leading to the inefficient exclusion of a portion of the incident beam. The present invention eliminates overillumination by the light source to maximize the efficiency of the microscope. The background of the present invention (Page 1, lines 6-16) discusses the drawbacks of apparatuses like that disclosed by Hara wherein the light source overilluminates an optical component. Thus, one skilled in the art looking to solve the problem of overillumination would not look to Hara for a solution. Neither Yamamoto nor Hara contain any teaching, suggestion, or motivation to eliminate

overillumination of a microscope component by a point-like source. Thus, Claim 17 would not have been obvious to one having ordinary skill in the art in light of the cited references.

Claims 25, 32, 33, and 39 are dependent on Claim 17 and include all of the limitations thereof. Consequently, Claims 25, 32, 33, and 39 are respectfully argued to be allowable for the reasons presented above concerning Claim 17.

Claims 22 and 23 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamoto in view of Hara et al. and further in view of Takagi et al. (United States Patent No. 5,140,458). The rejection is respectfully traversed for the following reasons.

Claims 22 and 23 both depend, directly or indirectly, from Claim 17. Consequently it is respectfully urged that these claims are allowable for the reasons stated above with respect Claim 17.

Claims 28 and 29 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamoto in view of Hara et al. with or without Dabbs et al. (United States Patent No. 5,054,926). The rejection is respectfully traversed for the following reasons.

Claims 28 and 29 both depend directly from Claim 17. Consequently it is respectfully urged that these claims are allowable for the reasons stated above with respect Claim 17.

Claims 34-36 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamoto in view of Hara et al. and further in view of Kato (United States Patent No. 4,530,578). The rejection is respectfully traversed for the following reasons.

Claims 34-36 all depend indirectly from Claim 17. Consequently it is respectfully urged that these claims are allowable for the reasons stated above with respect Claim 17.

Claim 37 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamoto in view of Hara et al. and further in view of Kato with or without Kain (United States Patent No. 5,672,880). The rejection is respectfully traversed for the following reasons.

Claim 37 depends indirectly from Claim 17. Consequently it is respectfully urged that this claim is allowable for the reasons stated above with respect Claim 17.

Claim 38 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamoto in view of Hara et al. and further in view of Dreessen et al. (United States Patent No. 5,404,238). The rejection is respectfully traversed for the following reasons.

Claim 38 recites, "a point-like light source operatively arranged to emit an illumination beam along said illumination beam path." Yamamoto discloses a laser source 1 that is not a point-like source. Dreessen discloses Xenon flashtube 20 as a light source, which is also not a point-like source. The Examiner has cited Hara et al. as disclosing a point-like source. However, there is no teaching, suggestion, or motivation in any of the cited references to combine their teachings to create the present invention. In fact, Hara teaches away from the present invention. Hara discloses an optical arrangement wherein light from source 2 is expanded and collimated before it is incident on pupil 5. The beam is rectangular before it is incident on the circular pupil 5. Thus, Hara clearly teaches overillumination of pupil 5, leading to the inefficient exclusion of a portion of the incident beam. The present invention eliminates overillumination by the light source to maximize the efficiency of the microscope. The background of the present invention (Page 1, lines 6-16) discusses the drawbacks of apparatuses like that disclosed by Hara wherein the light source overilluminates an optical component. Thus,

one skilled in the art looking to solve the problem of overillumination would not look to Hara for a solution. Neither Yamamoto, nor Hara, nor Dreessen contain any teaching, suggestion, or motivation to eliminate overillumination of a microscope component by a point-like source.

Further, not only is there no teaching, suggestion, or motivation in any of the cited references to create a microscope with a point-like source and zoom optical system arranged to steplessly modify the illumination diameter of the illumination beam, there is no teaching, suggestion, or motivation in any of the cited references to modify a microscope with a point-like source and zoom optical system arranged to steplessly modify the illumination diameter of the illumination beam to include an additional light input coupled into the illumination beam path, as claimed in Claim 38. Thus, Claim 38 would not have been obvious to one having ordinary skill in the art in light of the cited references.

In view of the foregoing, withdrawal of the rejections of Claims 17, 22, 23, 25, 28, 29, and 32-39 under 35 U.S.C. §103 is respectfully sought.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

17. (amended) An optical arrangement in an illumination beam path of a confocal laser microscope comprising:

a point-like light source operatively arranged to emit an illumination beam along said illumination beam path; and,

an illumination optical system arranged in said illumination beam path for modifying an illumination diameter of said illumination beam of said microscope, wherein said illumination optical system is a zoom optical system which operates steplessly, wherein said microscope includes a plurality of predefined objectives selectively positionable in said illumination beam path, and said illumination optical system is operatively arranged to modify said illumination diameter to match an entry pupil of a selected one of said plurality of objectives [and a focus of the zoom optical system remains at a location of said point-like source].

25. (amended) The optical arrangement according to claim [25] 24, wherein said illumination optical system is operatively arranged to automatically modify said illumination diameter.

38. (amended) An optical arrangement in an illumination beam path of a confocal laser microscope comprising:

a point-like light source operatively arranged to emit an illumination beam along said illumination beam path;

an illumination optical system arranged in said illumination beam path for modifying an illumination diameter of said illumination beam of said microscope, wherein said illumination optical system is a zoom optical system which operates steplessly [and a focus of the zoom optical system remains at a location of said point-like source]; and,

an additional input whereby a laser light beam from a further light source can be coupled in to said illumination beam path via an additional input and is adaptable to an entry pupil of an objective of said microscope with no adaptation of said actual illumination beam path.

Conclusion

It is respectfully urged that the present application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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MARKED UP VERSION TO SHOW CHANGES MADE

SUBSTITUTE SPECIFICATION

Optical Arrangement in the Illumination Beam Path of a Microscope

CROSS REFERENCES TO RELATED APPLICATIONS

[0001] The present application is the U.S. national phase under 35 U.S.C. 371 of International Patent Application No. PCT/DE99/00062 filed January 14, 1999 claiming priority of German Patent Application No. 198 01 833.9 filed January 14, 1998.

FIELD OF THE INVENTION

[0002] This invention relates to an optical arrangement in the illumination beam path of a microscope, in particular of a confocal laser microscope.

BACKGROUND OF THE INVENTION

[0003] In confocal laser microscopy, it has for some time been part of the existing art to expand the laser beam (which of itself is Gaussian) in the illumination beam path, by way of a suitable optical system, in such a way that the entry pupil of the respective objective or objectives usable there is fundamentally overilluminated. The degree of overillumination is an important design parameter. Overillumination of the entry pupil on the one hand provides homogeneous illumination thereof, the purpose being to guarantee the theoretical resolution, in particular in the case of objectives having different apertures. On the other hand, especially in the case of objectives with a small entry pupil, overillumination of the entry pupil results in considerable losses of excitation light. Such losses of excitation light are, however, not acceptable in applications where performance reserves in the excitation light are low.

[0004] The Leica TCS laser scanning microscope, for example, in which a fixed expansion optical system is provided, has become known from practical use. The diameter of

the laser beam expanded therein is approximately 25 mm ($1/e^2$ value) at the microscope objective.

[0005] The divergence of the laser light and thus the illumination of the aperture that is effective for the excitation light can be controlled by modifying the size of the excitation pinhole. Reference is made in this context, solely by way of example, to G.J. Brakenhoff et al. in Confocal Microscopy Handbook, J. Pawley, ed., 1994, pp. 87-91.

[0006] A PL APO 40X/1.25 objective, for example, has an entry pupil approximately 12 mm in diameter. A PL APO 100X/1.4 objective, on the other hand, has an entry pupil only 5 mm in diameter. As a result, in the latter the excitation light is lost by a factor of $(12/5)^2 = 5.76$ due to unnecessary overillumination.

[0007] Even if the beam path before the excitation pinhole is otherwise unchanged, the pinhole transmission in proportion to the area of the pinhole is characterized by corresponding light losses at small diameters. This, too, is unacceptable for practical use.

SUMMARY OF THE INVENTION

[0008] It is thus the object of the present invention to describe an optical arrangement in the illumination beam path of a microscope in which optimum illumination is guaranteed while reducing losses of excitation light.

[0009] The optical arrangement of the generic type according to the present invention achieves the aforementioned object by way of [the features of Claim 1. According to this,] an optical arrangement [of this kind is] characterized by an illumination optical system, arranged in the illumination beam path, to modify the illumination diameter.

[0010] According to the present invention, it has been recognized that the illumination diameter of the illumination beam should be more or less exactly adapted to the entry pupil of the objective in question in order to avoid light losses. Achieving this requires an illumination optical system, arranged in the illumination beam path, with which the

illumination diameter can be modified or adapted. In this manner, light losses such as those of the existing art mentioned above can be at least largely avoided.

[0011] Concretely, the illumination optical system provided according to the present invention could be embodied as an arrangement of replaceable fixed optics. When an objective is replaced, the fixed optics in the illumination beam path would correspondingly need to be replaced, so that the illumination diameter is matched to the entry pupil of the respective objective.

[0012] In very particularly preferred fashion, the illumination optical system comprises a variable optical system, preferably operating steplessly, so that it is unnecessary to replace fixed optics in the illumination beam path. The variable optical system can be a preferably motorized zoom optical system, which in turn can be embodied as an ordinary zoom optical system such as is used, for example, in commercially available video cameras.

[0013] For simple and optimum adaptation of the illumination diameter to the entry pupils of multiple objectives, an automatic adjustment system could be provided. Concretely, the modification in the illumination diameter could be matched to the entry pupils of predefined objectives, preferably arranged in a revolving nosepiece, the modification or adaptation being accomplished automatically depending on the particular objective being used (corresponding to the position in the nosepiece).

[0014] In terms of concrete potential applications of the optical arrangement according to the present invention, it is conceivable for the illumination optical system to be arranged downstream from a point light source or an optical fiber. The illumination optical system could be embodied as a parallelizing optical system with [a fixed focal intercept but variable focal length,] the beam diameter being adaptable to the entry pupil of the objective.

[0015] It is also conceivable for the illumination optical system to be embodied as an expanding optical system for a preferably directly coupled-in laser beam. [In this context the beam could be variably expandable in accordance with the ratio f_1/f_2 of the focal lengths.]

[0016] It has already been explained above by way of example that overillumination has been accepted in the existing art, especially when objectives have small entry pupils. The edge illumination in such cases, however, was certainly good. In order to promote edge illumination when an arrangement according to the present invention is used, it is advantageous, in particular with large entry pupils, if the illumination optical system comprises a further optical component that influences or favors edge illumination, the overillumination known from the existing art being avoided in any case. An optical component of this kind could be embodied as an additional lens, as an annular stop, or as a holographically generated optical element, the principal result thereof being that the ordinarily Gaussian laser beam is expanded in the edge regions. For example it would be possible thereby, especially in the case of confocal laser scanning microscopy, to achieve a constant intensity distribution over the entire entry pupil without causing substantial overillumination of the entry pupil of the objective. An intensity profile deviating therefrom may also be advantageous for a specific application.

[0017] It is furthermore conceivable to provide, in the case of the arrangement according to the present invention, an additional input for feeding in a further light source, this preferably involving the coupling-in of a laser light beam. With no modification of the actual illumination beam path, this laser light beam could be adaptable to the entry pupil of the objective, thus also making possible in this context an optimization of the laser light beam with no adaptation of the actual illumination beam path.

[0018] Lastly, an arrangement of the aforesaid kind could advantageously be used in multiphoton laser scanning microscopy or for multiphoton excitation.

[0019] There are various ways of advantageously embodying and developing the teaching of the present invention. Reference is made, for that purpose, [on the one hand to the claims which follow Claim 1, and on the other hand] to the explanation below of [three] several exemplary embodiments of the invention with reference to the drawings. In conjunction with the explanation of the preferred exemplary embodiments of the invention, a general explanation is also given of preferred embodiments and developments of the teaching. [The drawings show]

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] The subject matter of the invention is described with reference to the embodiment shown in the drawings:

Fig 1 shows, in a schematic depiction, a first exemplary embodiment of an optical arrangement according to the present invention in the beam path of a confocal scanning microscope, a point light source being provided as the light source and the scanning microscope being depicted, for the sake of simplicity, merely schematically by way of its components;

Fig. 2 shows, in a schematic depiction, a second exemplary embodiment of an optical arrangement according to the present invention in the beam path of a confocal scanning microscope, an optical fiber being provided as the light source and the scanning microscope being depicted, for the sake of simplicity, merely schematically by way of its components; [and]

Fig. 3 shows, in a schematic depiction, a third exemplary embodiment of an optical arrangement according to the present invention in the beam path of a confocal scanning microscope, a laser light source or laser beam being provided as the light source and the scanning microscope being depicted, for the sake of simplicity, merely schematically by way of its components;[.]

Fig. 4 shows, in a schematic depiction, another exemplary embodiment generally similar to that shown in Fig. 1 but further including an optical component in the illumination beam path for altering an intensity distribution of the illumination beam;

Fig. 5 shows, in a schematic depiction, another exemplary embodiment generally similar to that shown in Fig. 3, wherein a laser light beam from a further laser light source is coupled into the illumination beam path; and

Fig. 6 shows, in a schematic description, another exemplary embodiment generally similar to that shown in Fig. 3, wherein a plurality of objectives are selectively positionable in the beam path.

DETAILED DESCRIPTION OF THE INVENTION

[0021] FIGS. 1 through 3 each show an optical arrangement in the illumination beam path 1 of a confocal scanning microscope, the scanning microscope as a whole being depicted merely schematically for the sake of simplicity.

[0022] While in FIG. 1 a point light source 2 is depicted (symbolically) as the light source, in FIG. 2 the light is coupled in via an optical fiber 3. In the exemplary embodiment in FIG. 3, a laser beam 4 or a parallel light beam of an alternative/conventional light source is coupled via a lens 5 directly into illumination beam path 1.

[0023] According to the present invention, in all three exemplary embodiments (FIGS. 1, 2, and 3) an illumination optical system 6 is arranged in illumination beam path 1. This illumination optical system 6 serves to modify illumination diameter 7, thus making it possible for illumination diameter 7 to be adapted to the (symbolically depicted) entry pupil 8 of objective 9.

[0024] For better comprehension, the Figures show not only illumination beam path 1 as far as object 10, but also a scanner 12 and a beam combiner 11 arranged in illumination beam path 1.

[0025] A pinhole optical system 14 and a detection pinhole 15 (depicted schematically) are arranged in detection beam path 13.

[0026] In the exemplary embodiments depicted in FIGS. 1 and 2, illumination optical system 6 is embodied as a steplessly operating variable optical system. More precisely, in this case it is a motorized zoom optical system that, however, is shown merely symbolically by way of a shiftable lens 16. Concretely, what is being discussed here is an ordinary zoom optical system such as is known from video cameras.

[0027] In the embodiment depicted in FIG. 3, illumination optical system 6 is preceded by a lens 5 into which laser beam 4 is directly coupled.

[0028] Fig. 4 shows an arrangement according to the present invention wherein the illumination optical system comprises a further optical component 17 in the illumination beam path that influences or favors edge illumination. Optical component 17 can be an additional lens, an annular stop, or a holographically generated optical element, the principal result thereof being that the ordinarily Gaussian intensity distribution of the laser beam is expanded in the edge regions. For example it would be possible thereby, especially in the case of confocal scanning microscopy, to achieve a constant intensity distribution over the entire entry pupil without causing substantial overillumination of the entry pupil of an objective. An intensity profile deviating therefrom may also be advantageous for a specific application.

[0029] Fig. 5 shows an arrangement according to the present invention having an additional beamsplitter input 18 for feeding in a further light source 19, preferably providing a laser light beam. With no modification of the actual illumination beam path, this laser light

beam could be adaptable to the entry pupil of the objective, thus also making possible in this context an optimization of the laser light beam with no adaptation of the actual illumination beam path.

[0030] Fig. 6 shows an exemplary embodiment wherein a plurality of objectives 9, 9A, and 9B, respectively, are mounted on carrier 20. Carrier 20 is operatively arranged for axial movement in the direction of the arrow, to selectively position the plurality of objectives in the beam path.

[0031] To avoid repetition, reference is made to the general portion of the Specification regarding further features not evident from the Figures.

[0032] The invention has been described in detail with particular reference to certain preferred embodiments thereof, but it will be understood that variations and modifications can be effected within the spirit and scope of the invention.

Parts List

1 Illumination beam path
2 Point light source
3 Optical fiber
4 Laser beam
5 Lens (downstream from the laser beam)
6 Illumination optical system
7 Illumination diameter
8 Entry pupil of the objective
9 Objective
10 Object
11 Beam combiner
12 Scanner
13 Detection beam path
14 Pinhole optical system
15 Detection pinhole
16 Lens (of the illumination optical system)

ABSTRACT

An optical arrangement in the illumination beam path (1) of a microscope, in particular of a confocal laser microscope, is characterized, for optimum illumination while reducing losses of excitation light, by an illumination optical system (6), arranged in the illumination beam path (1), to modify the illumination diameter (7).